is at least partially coated with a solidified matrix consisting of a water-soluble polymer having a melting temperature less than that of the pharmaceutical agent. Claim 1.

The pharmaceutical agent of the present invention is in the "crystalline particulate form". (Claim 1) In contrast, Tanaka et al. discloses a medicinal particle described as "...any medicinal material [in] the form of powder or particle may be used." (Column 2, lines 47-48). The claimed invention does not use a medicinal particle in the powder form but rather a pharmaceutical agent in the crystalline particulate form. Tanaka does not teach crystalline particles.

The present invention provides for an enhanced compound dissolution rate of a "sparingly water-soluble pharmaceutical agent in crystalline form" (Claim 1) in water and thus affords improved bioavailability of the compound. The method of the instant invention "...uses water- soluble polymers such as polyvinylpyrrolidone, hydroxypropyl cellulose, or hydroxypropyl methylcellulose as carriers. The use of these water-soluble carriers improves the wettability of the poorly water-soluble crystalline pharmaceutical agents, thus improving the rate of their dissolution following administration..." (Page 2, lines 2-6). Also, "The polymer also must be sufficiently water soluble to allow dissolution of the particulate dispersion at a rate that provides the desired oral bioavailability and resulting therapeutical benefit." page 4, lines 30-33 and page 5, line 1 of the Specification. In contrast, Tanaka et al. disclose using a granulating-coating apparatus capable of coating the surface of a medicinal particle or powder with a liquid water insoluble material. Furthermore, as already noted by the Examiner, Tanaka et al. disclose prolonged release material. Specifically, Tanaka et al. teaches "A prolonged release dosage form of drug made by coating a surface of an ungranulated medicinal particle with a water-insoluble material which is physiologically acceptable and does not dissolve in water and gastric juice..." Abstract. Tanaka et al. sets out to "...provide a prolonged release dosage form having excellent prolonged release effect." Column 2, lines 22-24, thus teaching away from the claimed invention. Tanaka et al. do not teach enhanced compound dissolution rate of a "sparingly water-soluble pharmaceutical agent in crystalline form" as required by the Claimed invention.

The claimed invention is a pharmaceutical agent "...in crystalline form, wherein said particulate is at least partially coated in a solidified matrix..." (Claim 1). Moreover, the present invention "provides for mixing or extruding the active ingredients in solid particulate form with the polymeric carrier at a temperature at which the polymer softens, or even melts, but the drug remains solid or crystalline. The crystalline drug particles thus become coated and produce a product that is matrix coated..."(Page 2, lines 8-11 of the specification). In the present invention the compound, polymeric carrier, plasticizer, excipient, surfactant are dissolved or suspended and then fed into a mixer such as an extruder with one or more heating zones. The mixture is then melt extruded under heating temperatures that do not affect the stability of the drug, and is collected as a melt extrudate. This extrudate is a matrixed coated particulate dispersion that can be further processed, such as ground into a powdery mass, encapsulated, or pressed into tablets (page 6 of the specification). The crystalline drug particles of the claimed invention are embedded in a polymeric matrix. In contrast, Tanaka et al. do not disclose "crystalline particles coated with a solidified water-soluble polymer" of the claimed invention, rather Tanaka et al. disclose the use of a water-insoluble material to film coat a powder or particulate medicinal. Tanaka et al. disclose a solid dispersion of polymer materials sprayed onto a powder or particulate drug material with a nozzle using air pressure but then never melt extrudes the mixture, a requirement of the claimed invention. The drug powder or particles of Tanaka et al. are jet film coated and are not in crystalline particles as required by the claimed invention. In fact, the granulating-coating apparatus of Tanaka et al. has "...a nozzle for powder material for supplying ungranulated medicinal particles and a nozzle...for liquid material for supplying a water-insoluble material. The medicinal particles are supplied through a feeder...and jetted from the nozzle...into the processing cylinder...by the pressure of air supplied from a compressed-air source..." (Col. 3, lines 12-17). Tanaka et al. coats a pharmaceutical agent with a film. Tanaka et al. does not require the pharmaceutical in crystalline particle form to be embedded in a solidified matrix.

For the foregoing reasons, Claim 1 and therefore dependent Claims 2-7 and 10 are not anticipated by Tanaka et al. under 35 U.S.C. 102(b).

Applicant asserts that the present invention as claimed is not anticipated by Tanaka et al. Accordingly, withdrawal of the rejection under 35 U.S.C. 102(b) is respectfully requested.

Claims 1-7 and 10 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Olefsky et al. in view of Tanaka et al. Applicant respectfully traverses the rejection and courteously submits that the invention embraced by Claims 1-7 and 10 is not prima facie obvious within the meaning of 35 U.S.C. 103(a).

The claimed invention teaches "...a pharmaceutical agent in crystalline particulate form, wherein said particulate is at least partially coated with a solidified matrix..." Claim 1. Nowhere does Olefsky et al. teach or suggest melting a crystalline form of a pharmaceutical agent into a matrixed coated particulate dispersion. Olefsky et al. disclose preparations of troglitazone that are blended or compressed.

The Examiner states that it would have been obvious to one of ordinary skill to deliver the compounds of Olefsky et al. with the vehicle of Grabowski et al. to achieve the beneficial effect of delayed release.

The pharmaceutical agent of the present invention is in the "crystalline particulate form". (Claim 1) Tanaka et al. do not disclose a medicinal formulation wherein crystalline particles of a compound are melt extruded and consequently embedded in a polymeric matrix.

The present invention provides for an enhanced compound dissolution rate of a "sparingly water-soluble pharmaceutical agent in crystalline form" Claim 1. The invention of Tanaka et al. is intended to delay the release of a compound and, using the teaching of Tanaka et al., one would not arrive at a formulation having a compound with an enhanced dissolution rate, which is a critical characteristic of the present invention. Tanaka et al. do not each an enhanced compound dissolution rate of a "sparingly water-soluble pharmaceutical agent in crystalline form." Tanaka et al. teach a medicinal formulation to delay the release of the pharmaceutical compound thus, Tanaka et al. teach away form the invention.

The Examiner states that it would have been obvious to one of ordinary skill to deliver the compounds of Olefsky et al. with the vehicle of Grabowski et al. to achieve the beneficial effect of delayed release.

The claimed invention relates to "[a] solid particulate pharmaceutical dosage form suitable for oral delivery comprising a sparingly water-soluble pharmaceutical agent..." Claim 1. The vehicle of Grabowski et al. achieves the beneficial effect of delayed release. Grabowski et al. disclose "[I]t is an object of the present invention to produce compositions which contain active substances and are in the form of solid particles and which have delayed and uniform release..." (Col 1, line 44-47); and wherein "...delayed release of the active substance is required."(Col 1, line 54-55). Grabowski et al. do not teach a solid particulate pharmaceutical dosage form suitable for oral delivery comprising a sparingly water-soluble pharmaceutical agent to enhance the dissolution rate of the compounds.

In view of the foregoing arguments, Applicant asserts that neither Olefsky et al. nor Grabowski et al. taken alone disclose the instant invention. Additionally, Applicant believes that combining the compounds of Olefsky et al. with the vehicle of Grabowski et al. would not arrive at the present invention, namely the enhanced dissolution of the crystalline particulate dosage form. Therefore, the instant invention is not obvious in light of Olefsky et al. in view of Grabowski et al. For the forgoing reasons, Claim 1 and dependent Claims 2-7 and 10 are not rendered obvious under 35 U.S.C. 103. Accordingly, withdrawal of the rejection is respectfully requested.

In summary, Applicant's invention is a pharmaceutical formulation wherein the medicinal is in a crystalline form and is melt extruded with a polymeric coating useful in achieving an enhanced dissolution rate of the compound. None of the references anticipate the present invention under 35 U.S.C. 102(b). The references taken alone or in combination fail to render the claimed invention obvious under 35 U.S.C. 103, and the rejection of Claims 1-7 and 10 thereunder is therefore in error and should be withdrawn.

Applicant courteously requests the Examiner to reconsider the application in light of the foregoing comments, to withdraw the rejection of Claims 1-7 and 10 under 35 U.S.C. 102(b) and 35 U.S.C. 103(a), and to pass the case to issue.

Respectfully submitted,

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